REMARKS

Status of the Claims

Claims 15-28 are pending in this application, and Claims 15-19 and 21-28 stand rejected. Claims 16 and 20 are objected to as to form.

Objection to Claims 16 and 20

Claims 16 was objected to as to form. Applicants have adopted the Examiner's suggested amendment for Claim 16 for removing this objection, and thank Examiner Gilpin for suggesting this amendment. Accordingly, Applicants respectfully request that this objection be removed, and Claim 16 be allowed.

Claim 20 was also objected to as being dependent upon a rejected base claim. Applicants have entered new Claim 29 that corresponds to Claim 20 written in independent form and incorporating the elements of Claim 15 from this Claim 20 depends. Respectfully, Applicants submit that, as the Examiner indicates in the Office Action, new Claim 29 is allowable, and such action is requested.

Further, Applicants maintain that, as provided in the arguments presented herein, that Claim 15 is allowable, therefore Claim 20 has not been canceled. Accordingly, Applicants respectfully request that the objection to Claim 20 be removed, and Claim 20 be allowed.

Rejection of Claim 17 under 35 U.S.C. § 112, Second Paragraph

Claims 17 is rejected under 35 U.S.C. § 112 as being indefinite. The Examiner states that the language as written in Claim 17 is confusing, and suggests rewriting the claim with fewer "or" statements. By the amendment entered above in Claim 17, Applicants have made amendments where appropriate, to provide a claim of greater clarity. Accordingly, Applicants believe these amendments make Claim 17 definite, and respectfully request that this rejection be removed, and this claim allowed.

Rejection of Claims 15-17, 21, and 23 under 35 U.S.C. § 102(b)

Claims 15-17, 21 and 23 are rejected under 35 U.S.C. § 102(b) as being anticipated by Bruchman (WO 95/29712), as follows.

Claim 15. It is the Examiner's position that Bruchman discloses a synthetic base material with a layer of cells, constituting a hemocompatible surface, and an extracellular matrix, constituting a constituent of an outer layer of a mesothelial cell, thereby anticipating Claim 15. Applicants respectfully traverse this rejection as follows.

Bruchman describes a hemocompatible surface comprising a synthetic base material, a first layer of cells (typically smooth muscle cells or SMC), and a subendothelial matrix layer which serves as the direct blood contact surface. *See:* Claim 1; page 6, line 32-page 7, line 2.

The present invention according to Claim 15 does not recite a first layer of cells, nor a subendothelial matrix layer, nor does it recite cells of any type. Instead, the present invention comprises the *constituents* of the outer layer of blood cells or mesothelial cells as

components of a hemocompatible surface. Further the constituents of the outer layer of blood cells or mesothelial cells of the Applicants' invention are different from, and therefore not anticipated by, Bruchman's subendothelial matrix.

Respectfully, Applicants submit that Bruchman does not anticipate Claim 15, and request that this rejection be removed and this claim be allowed.

Claim 16. It is the Examiner's position that Bruchman discloses that the hemocompatible surface could include cells from a xenogenic source on its surface, thereby anticipating Claim 16. Applicants respectfully traverse this rejection as follows.

Bruchman's hemocompatible surface comprising a synthetic base material, a first layer of cells (typically SMC), and a subendothelial matrix layer which serves as the direct blood contact surface. *See:* Claim 1; page 6, line 32-page 7, line 2. The present invention according to Claim 16 does not recite a first layer of cells, nor a subendothelial matrix layer, nor does it recite cells of any type. Instead, the present invention comprises the *constituents* of the outer layer of blood cells or mesothelial cells as components of a hemocompatible surface. Therefore, regardless of whether Bruchman's hemocompatible surface includes cells from a xenogenic source on its surface, Claim 16 does not recite a layer of cells. Further the constituents of the outer layer of blood cells or mesothelial cells of the Applicants' invention are different from, and therefore not anticipated by, Bruchman's subendothelial matrix.

Respectfully, Applicants maintain that Bruchman does not anticipate Claim 16, and request that this rejection be removed and this claim be allowed.

Claim 17. It is the Examiner's position that Bruchman discloses that the cells of the hemocompatible surface could be endothelial cells, thereby anticipating Claim 17. Applicants respectfully traverse this rejection as follows.

Bruchman's hemocompatible surface comprising a synthetic base material, a first layer of cells (typically SMC), and a second subendothelial matrix layer which serves as the direct blood contact surface. *See:* Claim 1; page 6, line 32-page 7, line 2. The present invention according to Claim 17 does not recite a first layer of cells, nor a subendothelial matrix layer, nor does it recite cells of any type. Instead, the present invention comprises the *constituents* of the outer layer of blood cells or mesothelial cells as components of a hemocompatible surface. Therefore, regardless of whether Bruchman's hemocompatible surface includes endothelial cells, Claim 17 does not recite a layer of cells. Further the constituents of the outer layer of blood cells or mesothelial cells of the Applicants' invention are different from, and therefore not anticipated by, Bruchman's subendothelial matrix.

Respectfully, Applicants submit that Bruchman does not anticipate Claim 17, and request that this rejection be removed and this claim be allowed.

Claim 21. It is the Examiner's position that Bruchman discloses that the hemocompatible surface is substantially non-thrombogenic, thereby anticipating Claim 21. Applicants respectfully traverse this rejection as follows.

Bruchman's hemocompatible surface comprises a synthetic base material, a first layer of cells (typically SMC), and a second subendothelial matrix layer which serves as the direct blood contact surface. *See:* Claim 1; page 6, line 32-page 7, line 2. As discussed above, the Applicants' invention according to Claim 21 does not recite a first layer of cells, nor a

subendothelial matrix layer, nor does it recite cells of any type. Instead, the present invention comprises the *constituents* of the outer layer of blood cells or mesothelial cells as components of a hemocompatible surface. Therefore, regardless of whether Bruchman's hemocompatible surface is substantially non-thrombogenic, Claim 21 does not recite a layer of cells. Further the constituents of the outer layer of blood cells or mesothelial cells of the Applicants' invention are different from, and therefore not anticipated by, Bruchman's subendothelial matrix.

Respectfully, Applicants submit that Bruchman does not anticipate Claim 21, and request that this rejection be removed and this claim be allowed.

Claim 23. It is the Examiner's position that Bruchman discloses that an article such as a heart valve comprises a hemocompatible surface, thereby anticipating Claim 23. Applicants respectfully traverse this rejection as follows.

Bruchman's heart valve comprises a hemocompatible surface comprising a synthetic base material, a first layer of cells (typically SMC), and a second subendothelial matrix layer which serves as the direct blood contact surface. *See:* Claim 1; page 6, line 32-page 7, line 2. The heart valve according to Claim 23 comprises a hemocompatible surface that does not comprise a first layer of cells, nor does it comprise a subendothelial matrix layer, nor does it comprise cells of any type. Instead, the hemocompatible surface of the present invention comprises the *constituents* of the outer layer of blood cells or mesothelial cells. Further, Claim 23 does not recite a layer of cells. Accordingly, the constituents of the outer layer of blood cells or mesothelial cells of the Applicants' invention are different from, and therefore not anticipated by, Bruchman's article such as a heart valve comprising a subendothelial matrix.

Accordingly, Applicants respectfully maintain that Bruchman does not anticipate Claim 23, and request that this rejection be removed and this claim be allowed.

Rejection of Claims 22 and 23 under 35 U.S.C. § 103(a)

Claims 22 and 23 stand rejected under 35 U.S.C. § 103(a) as being obvious in view of the combination of Bruchman (WO 95/29712) and Minuth (U.S. Patent No. 6,187,053). It is the Examiner's position (paragraph no. 5, pages 3-4 of the Office Action) that Bruchman teaches a hemocompatible surface which, when combined with Minuth's teaching of a porous carrier comprising a metal, renders these claims obvious. Applicants respectfully traverse this rejection as follows.

Bruchman's hemocompatible surface comprises a synthetic base material, a first layer of cells (typically SMC), and a second subendothelial matrix layer which serves as the direct blood contact surface. *See:* Claim 1; page 6, line 32-page 7, line 2. Therefore, even if Bruchman is combined with Minuth, the combined teachings cannot render Claims 22 and 23 obvious, because Applicants' invention does not comprise a first layer of cells, nor a subendothelial matrix layer, nor any analogous layers. Instead, the present invention comprises a *material* (an artificial, organic, or inorganic compound), and the *constituents* of the outer layer of blood cells or mesothelial cells as components of a hemocompatible surface.

The combined references do not teach or suggest that Bruchman's first layer of cells could be completely eliminated, nor is there any suggestion in the references themselves or in the knowledge of one of ordinary skill, that the subendothelial matrix of Bruchman could be replaced by Applicants' cell constituents of the outer layer of blood cells or mesothelial cells.

Respectfully, Applicants maintain that the combination of Bruchman and Minuth does not teach or suggest the invention recited in Claims 22 and 23, and therefore request that this rejection be removed and these claims be allowed.

Rejection of Claims 24-28 under 35 U.S.C. § 103(a)

Claims 24-28 are rejected under 35 U.S.C. § 103(a) as being obvious in view of the combination of Keller (U.S. Patent No. 5,071,973) and Bruchman (WO 95/29712). It is the Examiner's position (paragraph no. 6, page 4 of the Office Action) that these claims are obvious because Keller teaches binding a biologically inert endothelial cell surface polysaccharide to a biopolymer, where the biopolymer is a hemocompatible surface. The Examiner further states that when combined with Bruchman's teaching of a hemocompatible surface where the cells employed are mesothelial cells, these claims are rendered obvious. Applicants respectfully traverse this rejection as follows.

Bruchman's hemocompatible surface comprises a synthetic base material, a first layer of cells (typically SMC), and a second subendothelial matrix layer which serves as the direct blood contact surface. *See:* Claim 1; page 6, line 32-page 7, line 2. Keller discloses the binding of the endothelial cell surface polysaccharide HS I to artificial surfaces to make the surface hemocompatible. *See:* Abstract; col. 1, lines 7-14. The polysaccharide HS I is a specific endothelial cell surface proteopolysaccharide, which is *only produced by endothelial cells*. Thus, Keller discloses the use of only one specific constituent of the outer layer of only one type of cell, namely, an endothelial cell.

Applicants respectfully submit that, even if Bruchman is combined with Keller, the combined teachings cannot render Claims 24-28 obvious, because one of ordinary skill in the art would not be motivated to attempt to isolate the HS I polysaccharide from mesothelial or blood cells, nor would one of ordinary skill be motivated to use the *entire mixture* of all polysaccharide constituents of the outer layer of mesothelial or blood cells to prepare a hemocompatible surface, as Applicants have done. There is no teaching or suggestion in the references themselves or in the knowledge of one of ordinary skill, that the subendothelial matrix of Bruchman—or any portion of Bruchman's surface—could be replaced by the *entire mixture* of all polysaccharide constituents of the outer layer of mesothelial or blood cells, as in Claims 24-28.

Respectfully, Applicants maintain that Bruchman and Keller do not teach or suggest Applicants' invention as recited in Claims 24-28, and therefore request that this rejection be removed and these claims be allowed.

Rejection of Claims 18 and 19 under 35 U.S.C. § 103(a)

Claims 18 and 19 stand rejected under 35 U.S.C. § 103(a) as being obvious in view of the combination of Bruchman (WO 95/29712) and U.S. Patent No. 6,156,572 to Bellamkonda et al. (Applicants respectfully note that this U.S. Patent is to Bellamkonda et al. rather than to Hubbell, as the Office Action indicated.) It is the Examiner's position that Bruchman teaches a hemocompatible surface that incorporates an extracellular matrix material, and that, when combined with Bellamkonda's teaching of a bio-artificial extracellular matrix including heparin sulfate and chondroitin sulfate that can be implanted as a hemocompatible

surface, this combination renders these claims obvious. Applicants respectfully traverse this rejection as follows.

Bruchman's hemocompatible surface comprises a synthetic base material, a first layer of cells (typically SMC), and a second subendothelial matrix layer which serves as the direct blood contact surface. *See:* Claim 1; page 6, line 32-page 7, line 2. Bellamkonda discloses that most cells in multicellular organisms have an extracellular matrix, that may comprise glycosaminoglycans and proteoglycans such as chondroitin sulfate and heparin sulfate. However, all glycosaminoglycans and proteoglycans such as these often exhibit very different properties depending upon their origin, for example liver heparin sulfate shows a considerable coagulation-activating effect, whereas erythrocyte surface heparin sulfate is marked by being completely athrombogenic.

Applicants respectfully note that the present invention uses only cellular constituents with specific properties, and from certain well-defined sources, namely from blood cells or mesothelial cells. Thus, Applicants have unexpectedly discovered that cellular constituents obtained specifically from the athrombogenic surfaces of blood cells or mesothelial cells are effective in the hemocompatible surfaces of the present invention, whereas glycosaminoglycans and proteoglycans from all sources are not. For example, chondroitin sulfate obtained from cartilage is not hemocompatible and cannot be used in the present invention, whereas chondroitin sulfate obtained from the outer layers of blood or mesothelial cells is athrombogenic and is hemocompatible.

Therefore, even if Bruchman is combined with Bellamkonda, the combined teachings cannot render Claims 18 and 19 obvious, because one of ordinary skill in the art would

not be motivated to select, from among all the possibilities, glycosaminoglycans and proteoglycans obtained only from mesothelial or blood cells, as Applicants have done. Further, the combined references also do not teach or suggest that Bruchman's first layer of cells could be completely eliminated, nor is there any suggestion in the references themselves or in the knowledge of one of ordinary skill, that the subendothelial matrix of Bruchman could be replaced by Applicants' *constituents* of the outer layer of blood cells or mesothelial cells.

Respectfully, Applicants maintain that Bruchman and Bellamkonda do not teach or suggest Claims 18 and 19, and therefore request that this rejection be removed and these claims be allowed.

Conclusion

Applicants believe the remarks herein place the claims in condition for allowance. Accordingly, such action is respectfully requested.

No additional fees are believed due, however, the Commissioner is hereby authorized to charge any deficiencies which may be required, or credit any overpayment, to Deposit Account Number 11-0855.

Early and favorable consideration is respectfully solicited. If the Examiner believes any informalities remain in the application that can be resolved by telephone interview, a telephone call to the undersigned attorney is earnestly solicited.

Respectfully submitted,

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